AMENDMENTS TO THE SPECIFICATION

Applicants attach hereto new pages 2, 4-6, and 10-12 making corrections to the Specification.

[0003] The components of the arterial wall that are primarily responsible for its mechanical strength and elasticity are the structural proteins collagen and elastin. Collagen, which serves a protective function, is very extensible and breaks at a stress of about 500 megapascals. Collagen is the substance that gives the artery wall its high resistance to the hemodynamic forces created by the heart pumping the blood through the vessel. Elastin fibers, on the other hand, can stretch to about 250% of their original length and have about 20 times lower modulus of elasticity than collagen. These two proteins cooperate to provide vessels with sufficient strength and flexibility to withstand the continuous pounding and pressure of the blood as it flows through the vessel in response to the beat of the heart.

[0004] A fully developed cerebral aneurysm, however, consists almost entirely of collagen fibers, because the majority of the elastin fibers are fragmented by the distending forces of blood pulsating through the vessel in response to the rhythmic beat of the heart. This loss of elastin fibers is especially true for the top of aneurysm, where the tissue degradation is more advanced than in the base and the sidewalls of the aneurysm. Most ruptures consequently occur at the top, or dome, of the aneurysm. The aneurysm ruptures when its wall become too thin to withstand circumferential stresses imposed by the pressure differential between the arterial lumen and the subarachnoid space outside the artery.

[0005] Each year about 30,000 North Americans are diagnosed with a ruptured aneurysm and more than half of them die within the first thirty (30) days thereafter. Diagnosis and successful treatment of an aneurysm prior to its rupture is therefore critical to improving the survivability of a patient to this disease. The fundamental objective in the management of an aneurysm that has not ruptured is to stabilize it, thus avoiding further dilatation or growth. Aneurysm stabilization is currently accomplished by:

the described methods is that the blood clot, formed by blood stagnation inside the cavity or its heating, is relatively weak. The fresh arterial blood, coming into the aneurysm can cause lysis (dissolution) of the clot inside the sac and create a chance that a piece of wire or a piece of clot can be displaced from the aneurysm into the blood stream and embolize distally.

[0012] A new treatment is needed that is free from these shortcomings and will improve the stabilization of aneurysms by improved methods and apparatus. The present invention provides an apparatus and method that stabilizes aneurysms of different shapes and produces a clot that is much more resistant to wash out by the blood flow.

SUMMARY OF THE INVENTION

[0013] The invention is an apparatus and method for forming a mural arterial thrombus, that is, a thrombus grown on and attached to the vascular wall inside a cerebral aneurysm, with emphasis on the formation of the arterial thrombus on the inner surface of the dome and the neck of the aneurysm.

[0014] In the present invention, formation of the desired arterial thrombus begins with an injury to the endothelium of the vascular wall of the aneurysm. This injury, which triggers the coagulation sequence within an aneurysm, is created by ultraviolet (UV) radiation delivered to the inner surface of the aneurysm by a micro catheter. The micro catheter comprises a steerable guide wire with an optical fiber in it. The proximal end of the optical fiber is coupled to a laser capable of producing (UV) radiation. The distal end of the guide wire, which emits UV radiation scattered in different directions, is placed inside the aneurysm. A dose of UV radiation, sufficient to cause complete necrosis of the endothelium and lead to the formation of the [arteriala] arterial thrombus, is delivered to the whole surface of the aneurysm.

[0015] Preferably, the blood is displaced from the aneurysm by a UV radiation transparent fluid, such as saline. Saline for this purpose may be delivered into the aneurysm from a pressurized saline bag or by a pump outside the patient via a plastic micro tube placed over the guide wire. In one implementation of the present invention a soft balloon, secured around the plastic micro tube, temporarily occludes the artery, thus ensuring better transparency inside the aneurysm. After delivery of the appropriate dose of UV radiation, the saline wash is terminated allowing blood to flow again into the aneurysm.

[0016] In another implementation of the invention an optical fiber (or multiple fibers) is placed inside the wall of the plastic micro tube delivering saline to the aneurysm. In this case a conventional guide wire is used for placing the tip of the micro catheter inside the aneurysm, and the blood flow in the feeding artery is not occluded even temporarily. The UV radiation is delivered to the aneurysm wall in the same manner as in the first implementation.

[0017] The foregoing method also may be used for the [treatment] <u>treatment</u> of AVMs and arterial fistulas.

[0018] The foregoing objects of the invention will become apparent to those skilled in the art when the following detailed description of the invention is read in conjunction with the accompanying drawings and claims. Throughout the drawings, like numerals refer to similar or identical parts

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] FIG. 1 illustrates an apparatus for treatment of cerebral aneurysms in accord with the present invention.

[0020] FIG. 2 is a cross-section taken along viewing plane 2-2 of FIG. 1.

[0021] FIG. 3 presents a detailed view of the distal end of a catheter in accord with the present invention.

[0022] FIG. 4 depicts another embodiment of an apparatus for treatment of cerebral aneurysms in accord with the present invention.

[0023] FIG. 5 is a cross sectional view of the embodiment shown in FIG. 4 taken along viewing plane 5-5.

[0024] FIGS. 6A, 6B, and 6C shows several stages of treatment of an aneurysm.

[0025] FIG. 7 shows the treatment of arterial venous malformations using an apparatus in accord with the present invention.

DESCRIPTION OF PREFERRED EMBODIMENT

[0026] An apparatus 10 for treatment of an aneurysm and in accord with the present invention is schematically shown in FIGS. 1 and 2. Apparatus 10 comprises a laser 12, a steerable guide wire 14, and a catheter 16. Catheter 16 will be appropriately sized depending upon where in the patient's body a treatment will occur. For treatment of a cerebral aneurysm, which may require navigation through very small blood vessels in the brain, catheter 16 will be a microtube in the form of an elongated tube and may include a substantially centrally disposed tubular passage 18 defined by a wall 20 for receiving guide wire 14. Catheter 16 may, as shown in FIG. 1, also include an expandable balloon 21, which is used for occluding an artery during an interventional surgical procedure. Catheter 16 may also include a channel 22 disposed in the catheter wall 24 that is in fluid communication with balloon 21.

shows an artery 150 with an aneurysm 152. The aneurysm dome 154 reveals a thinner vessel wall 156 as a result of the distention of the vessel 150 at that location. Blood flow is indicated generally by arrow 158.

[0038] FIG. 6B illustrates the aneurysm following treatment with the present invention. It will be observed that a necrotized layer 160 of endothelial cells has been formed following treatment with UV radiation on the inside surface of the aneurysm.

[0039] FIG. 6C illustrates the aneurysm 152 after the formation of a "real arterial thrombus" 164. At the dome the thickness of the aneurysm's wall is the lowest and the probability of rupture is the highest (about 90% of all cerebral aneurysms are ruptured at the dome). Narrowing the neck of the aneurysm causes a decrease in the blood pressure within the aneurysm sac and thus assists in its stabilization. A "real arterial thrombus" significantly differs from a blood clot, as that term is usually used in the described methods of stabilization of aneurysms. The underlying core of the arterial thrombus consists of fibrin and aggregated platelets, which strongly adhere to each other and to the arterial wall. The color of the core is white, so an arterial thrombus is sometimes referred to as a "white thrombus". The margin or exterior layer of the arterial thrombus consists of coagulated blood and is red. Arterial thrombi form at the site of an injury to the endothelium, which exposes the highly thrombogenic connective tissue underlying the endothelial layer to the blood flow. This connective tissue, primarily collagen, causes activation of platelets, leading to the formation of a thrombus.

[0040] Necrotic endothelial cells are not able to produce tissue plasmogen activator t-PA, major function of which is preventing thrombus formation on the vessel walls, and cannot stay attached to the the vessel wall surface. As they are flaked off and carried away by the blood flow, the highly thrombogenic underlying layer consisting of collagen is exposed. Platelets from blood, activated at the endothelium-denuded [from endothelium] surface of the aneurysm, start aggregation and the whole sequence of arterial thrombus formation on the irradiated

surface of the aneurysm is launched. In several days after intervention the thrombus, contracted in volume and ingrown by [capillaries] capillaries and fibroblasts, becomes organized. The fully organized thrombus on the inside surface of the aneurysm leaves a thick layer of fibrotic tissue, covered with a newly restored endothelial layer, thereby stabilizing the aneurysm against rupture and [further] further thrombosis.

[0041] The energy fluence, required for causing necrosis of the endothelial cells, falls in the range of several units to several hundreds of mJ/cm2, that is, within a range of about 5 to about 1000 mJ/cm2. The time required for achieving full necrosis of endothelial cells with a milliwatt UV laser, falls in the range of about 10 seconds to several minutes. It will be understood that the time period over which irradiating of the aneurysm with UV energy occurs is inversely dependent upon the applied energy. As the power of the applied radiation decreases, the duration of time over which the energy must be applied to cause the desired cell death increases and vice versa. An Argon ion laser, generating UV radiation with wavelength 257 nanometers or a Nd-YAG laser generating radiation with a wavelength 256 nanometers (the fourth harmonic of the infrared wavelength 1.06 microns) [is] are just two examples of UV radiation sources that can be used in accord with the present invention.

[0042] Without functioning endothelial cells the aneurysm's inner wall becomes highly thrombogenic, triggering formation of thrombus on it and coagulation of the blood in the sac of the aneurysm. After organization of the thrombus the inner wall of the aneurysm will be covered with a thick layer (several hundred microns) of a collagen rich fibrous tissue. For a normal artery the thickening of its wall is a negative event. It results in a loss of patency and flexibility of the vessel. But for an aneurysm the thickening of the wall decreases actual tensile stresses in it and arrests the growth of the aneurysm. It follows from a well-known fact that circumferential stress, responsible for the aneurysm rupture, is inversely proportional to the aneurysm wall thickness:

$$S=PR/2h$$

[0043] where

[0044] S=Circumferential Stress;

[0045] P=Blood Pressure;

[0046] R=Radius of the Aneurysm; and

[0047] h=Thickness of the Aneurysm Wall.

[0048] A several time increase in wall thickness causes a several time drop in the stresses. The formula is taken from "The Physics of Cerebrovascular Disease" by George J. Hademenos and Tarik F. Massoud, Springer--Verlag, 1998, ISBN 1-56396-558-5.

[0049] The critical thickness of a saccular aneurysm, at which a rupture occurs, is around 40-50 microns. The thickness of a fibrous layer after full organization of thrombus reaches several hundred microns, thus warranting stabilization of the aneurysm [after] by treatment with UV radiation.

[0050] FIG. 7 schematically illustrates treatment of an arterial venous malformation (AVM) 120 in accord with the present invention. AVMs are massive blood formations wherein one or more feeding arteries provide blood to the mass, which is then drained by one or more draining arteries without the blood ever being supplied to the tissue, typically cerebral tissue. The formation of the AVM, then, results in starvation of the surrounding tissues because of the diversion of the fresh arterial blood from the tissue by the AVM. As shown in the figure, guide wire 14 with an optical fiber 32 inside is advanced through a feeding artery 122 to AVM 120. The optical tip 36 of the fiber 32 is